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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/449,204	11/24/1999	ANTHONY H. DODGE	P1543R1	6001

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EXAMINER
FORMAN, BETTY J

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 09/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/449,204	SINICROPI ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 05 September 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.☒ A Notice of Appeal was filed on *05 September 2003*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.☐ The proposed amendment(s) will not be entered because:

(a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see Note below);

(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3.☐ Applicant's reply has overcome the following rejection(s): _____.

4.☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.

6.☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: *2,4,5,8-14,17-20 and 24-46*.

Claim(s) withdrawn from consideration: _____.

8.☐ The proposed drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9.☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10.☒ Other: *Continuation of Advisory Action*

Continuation of Advisory Action

1. Applicant argues that the office has relied on elements "well known in the art" to make a case of obviousness and therefore has not estabilished a prima facie case of obviousness as required.

Specifically, Applicant states that the office notes that Hendrickson et al do not teach the detector molecule is an aatemr and they do not teach the aptamer is quantitated or detected using real-time PCR. Applicant argues that "following this admission, the Examiner states that Gibson et al. teaches real time PCR using detectable non-primer probes **and without any citation from within the references asserts that the combination would be obvious simply because the use of real-time PCR was well known.**"

The argument has been considered. However, contrary to Applicant's assertion, the office has repeatedly provided motivation for combination of Hendrickson and Gibson. For example, in the Final Office Action, it is stated that:

"Gibson et al. teach a method for detecting a PCR amplified product with sequence-specific non-primer probes using real-time PCR (page 997, right column, page 1000, last paragraph and Table 1) wherein **the reaction is detected and quantitated every 8.5 seconds thereby providing accurate and time-sensitive information during the PCR reaction** (page 996, left column, lines 1-3). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the detection of Hendrickson et al. wherein aliquots of the PCR reaction are run on agarose gel for detection and quantitation of amplified product at a single time point (page 525, right column, second full paragraph) with the Gibson et al. method wherein the PCR reaction is detected and quantitated every 8.5 seconds (page 996, left column, lines 1-3) by detection of non-primer probe hybridization for the expected benefit of eliminating the agarose gel step and **for the expected benefit of accurate and time-sensitive detection as taught by Gibson et al. (page 995, right column, lines 1-5).**"

Therefore, Applicant's assertion that the Office has not provided citations or motivation taught in the cited art is incorrect. It is noted that Applicant has not argued the citations or motivation provided by the Office.

2. Applicant argues regarding Gold et al that the Office Action is "equally without a teaching to combine or a suggestion of success of such a combination." Again for Applicant's convenience, the citation from the Final Office Action is provided.

"aptamer detector molecules were well known in the art at the time the claimed invention was made as taught by Gold et al. (Column 8, lines 22-45) who teach that aptamers can be employed as antibodies; aptamers have conventionally been employed in detection assays; and aptamers have numerous advantages over antibodies i.e. **aptamers can be readily amplified, they do not require animal immunization and the binding affinity of aptamers can be tailored to users needs** (Column 8, lines 37-45). Therefore, It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the antibody-detector molecule of Hendrickson et al. with the aptamer-detector molecule of Gold et al. for the expected benefit of specific, qualitative and quantitative detection of target molecules as taught by Gold et al. (Column 27, lines 54-56) and for the additional benefits of aptamers i.e. **aptamers can be readily amplified, they do not require animal immunization and the binding affinity of aptamers can be tailored to used needs as taught by Gold et al. (Column 8, lines 37-45).**"

Therefore, Applicant's assertion that the Office has not provided citations or motivation taught in the cited art is incorrect. It is noted that Applicant has not argued the citations or motivation provided by the Office.

3. Applicant argues that while the instant invention teaches a washing step to remove nuclease, the Office Action refers to Hendrickson et al for a washing step which is not in concert with Applicant's invention because Hendrickson does not contemplate aptamer and would not be aware of or concerned with nuclease. In response to applicant's argument that Hendrickson does not contemplate removal of nuclease via a washing step, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). The claim is drawn to a method comprising "washing the ternary complex". Hendrickson teaches a washing the ternary complex. Therefore, Hendrickson meets the limitation of the method step. The fact that Applicant has recognized another advantage that would flow from the washing does not patentably distinguish the instant claim over the teachings of the cited prior art.

Furthermore, the instant specification teaches:

"The normal washing employed in the immuno-assay portion of the assay was sufficient to remove sufficient levels of endogenous nuclease so that the quantitation was not effected." (page 36, lines 18-20).

Therefore, normal washing employed by Hendrickson et al would remove nuclease as claimed.

4. Applicant also argues that the washing step of Gold et al is not directed to removal of nuclease. The argument has been considered but is not found persuasive because Gold et al teach washing the complexes prior to amplification as instantly claimed (Column 24, line 53-Column 25, line 9) whereby their method (comprising the wash step) produces amplifiable nucleic acids (Column 25, lines 10-54). Furthermore, as cited above, the courts have stated that the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious.

Therefore, because Gold et al teach a washing step; because Hendrickson et al teach a washing step; because the specification teaches that "normal washing" removes nuclease; and because the courts have stated that the fact that applicant has recognized another advantage does not distinguish over the prior art, the instantly claimed washing does not distinguish the instantly claimed invention over the prior art.

5. Applicant argues that Cubicciotti does not teach a washing step to remove nuclease. The argument has been considered but is not found persuasive as discussed above regarding Hendrickson and Gold. Specifically, Cubicciotti teach a washing step. The courts have stated that the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability. Furthermore, the instant specification teaches that "normal washing" removes nuclease (page 36, lines 18-20). Therefore, the washing step of Cubicciotti removes nuclease as instantly claimed.

6. Applicant argues that the "sole basis for combining the references....is that real-time PCR using detectable probes was well known in the art". The argument is not found persuasive because the Office has provided motivation for combination and because Applicant has not argued the motivation presented.

"Gibson et al. teach a method for detecting a PCR amplified product with sequence-specific non-primer probes using real-time PCR (page 997, right column, page 1000, last paragraph and Table 1). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply real time PCR of Gibson et al to the detection of Cubiccoitti and to detect and quantitate PCR products every 8.5 seconds (page 996, left

column, lines 1-3) by detection of non-primer probe hybridization for the expected benefit of eliminating the agarose gel step and for the expected benefit of **accurate and time-saving detection as taught by Gibson et al. (page 995, right column, lines 1-5)**."

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:30 TO 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
Primary Examiner
Art Unit: 1634
September 17, 2003